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Multitendon xanthomatosis in a normocholesterolemic patient

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We present a rare case of multisite xanthomatosis occurring in a 38-year-old normocholesterolemic man without a familial history. More commonly, these conditions are associated with familial hypercholesterolemia and cerebrotendinous xanthomatosis. Tendon xanthomas should prompt clinicians to perform a thorough investigation of the patient's metabolic panel and family history. Rarely, these conditions occur in patients without demonstrable dysmetabolic state. The characteristic MR imaging findings are presented in conjunction with review of the literature.

Introduction

A rare case of multitendon xanthomatosis occurred in a patient with a normal standard lipid panel. The association of xanthomatosis with familial hypercholesterolemia has been well established. It is not infrequent for patients to initially present with tendinous xanthomatous masses that subsequently alert clinicians to examine the cholesterol panel. However, in this case, the standard lipid profile was within normal range.

Case report

A 38-year-old right-hand-dominant man with no previous pertinent medical, surgical, or family history presented for imaging evaluation of a lump on the dorsum of his left hand at the level of the third metacarpophalangeal joint. He had an essentially normal metabolic serology panel, with only minimal LDL elevation and HDL depression (triglyceride 96 [nl <150], total cholesterol 188 [nl <200], HDL 34 [higher risk <40], LDL 135 [nl <130], VLDL 19 [nl <30], Hgb A1C 5.3 [nl <6.5], T4 9.3 [nl 4.5-10.9], and TSH 0.715 [nl 0.35-5.5]). Similar masses were noted in the pretibial soft tissues and the Achilles-tendon region, which had been stable for approximately five years.

Magnetic resonance imaging (MRI) of the middle finger (Fig. 1), pretibial area of the knee (Fig. 2), and Achilles tendon (Fig. 3) were performed. T1-weighted images demonstrated a speckled inhomogeneous appearance to the finger extensor tendon and Achilles tendon. This intratendinous increased signal interdigitated within the normally low-signal tendon fibers. The T2-weighted images also demonstrated this characteristic stippled appearance. Importantly, interdigitation helps to distinguish this condition from some other entities. However, the pretibial lesion (Fig. 2) did not interdigitate within the patellar tendon. The imaging findings supported the diagnosis of xanthomatosis.

At surgery, extra and intratendinous components were dissected from the dorsal aspect of the middle finger (Fig. 4). The specimen measured 2.0 x 2.0 x 0.8 cm. No extension into the MCP joint capsule was observed. Grossly, the lesion appeared yellow-tan and was somewhat firm and rubbery in texture. Subsequently, excision of the lesion from the pretibial soft tissues just ventral to the tibial tuberosity revealed similar appearing yellowish-tan, lobulated, rubbery tissue. Photomicrographs (Fig. 5) of the digital lesion demonstrated the accumulation of cholesterol and lipid foam cells interspersed among the normal tendon bundles. The pathologic diagnosis of both lesions confirmed cholesterol xanthomatosis.

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Figure 1. 38-year-old man with multitendon xanthomatosis. Top: Sagittal T1-weighted MRI of the third metacarpophalangeal (MCP) joint. Arrows indicate a lobulated low-intermediate signal lesion, both dorsal and associated with the extensor tendon. Above: Axial T1-weighted MRI at the level of the third metacarpal head (MC) showing the lesion (arrows). There is interdigitation of the mass with the underlying extensor tendon (long arrow).

Figure 2. 38-year-old man with multiple tendon xanthomatosis. Top: Sagittal T1-weighted MRI shows a pretibial lesion (arrow) at the level of the tibial tuberosity at and inferior to the distal insertion of the patellar tendon, with similar signal characteristics to the finger lesion. The patellar tendon appears normal. Above: Sagittal T2-weighted fat-suppressed MRI shows the lesion to be low in signal (arrows).

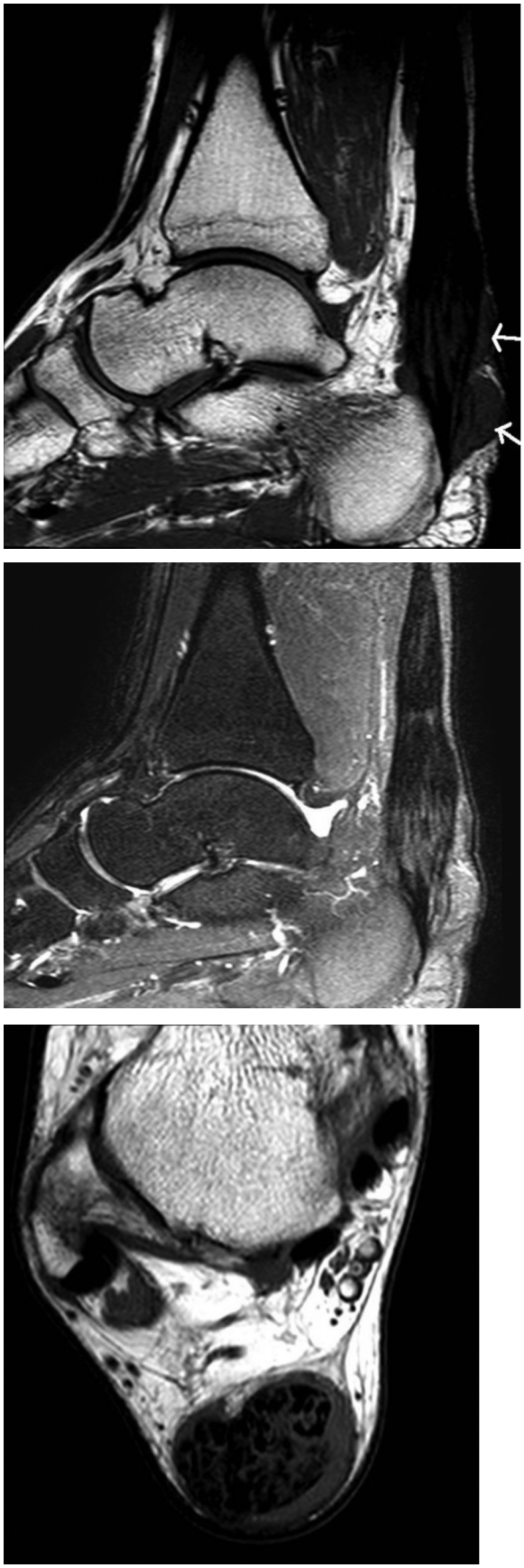

Figure 3. 38-year-old man with multitendon xanthomatosis. Top: Sagittal T1-weighted MRI of the ankle shows that the Achilles tendon is fusiformly enlarged, with both intratendinous vertical striations and more exophytic nodular masses (arrows). These masses are well visualized, in contrast to the surrounding fatty tissues. Middle: Sagittal T2-weighted fat-suppressed MRI demonstrates fusiform Achilles-tendon enlargement, with abnormal vertical striations interdigitating within the tendon as well as nodularity and abnormal signal around the tendon. The more exophytic nodular masses noted in the top image are less conspicuous on T2-weighted, fat-suppressed images. Bottom: Axial T1-weighted MRI of the Achilles tendon shows fusiform tendon enlargement, with interdigitating vertical striations and abnormal soft tissue around the tendon, predominately dorsomedial.

Discussion

Xanthomas are characterized by the accumulation of lipid-laden macrophages and other inflammatory cells in response to cholesterol deposition in tissues (1, 5). They are commonly associated with disorders of lipid metabolism. When present, they have a predilection for the extensor tendons of the hand, particularly the metacarpophalangeal joints of the fingers. The Achilles and patellar tendons can also be involved (2). Ninety per cent of patients with tendon xanthomas exhibit involvement of the extensor tendons of the hand, and the Achilles tendon is involved in about half the cases. Less commonly, the patellar tendon, plantar fascia, and triceps tendon can also be involved (3).

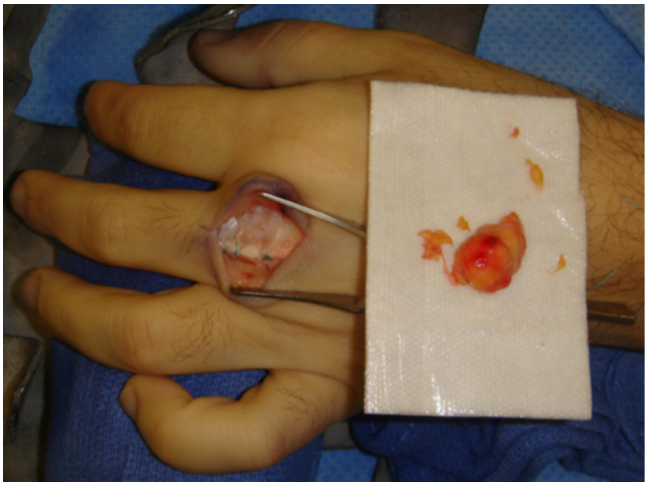

Figure 4. 38-year-old man with multitendon xanthomatosis. Intraoperative photograph with resected specimen from the middle finger-extensor region

Familial hypercholesterolemia (FH) is an autosomal dominant disorder associated with premature atheromatous coronary artery disease. Xanthomas arise in patients with

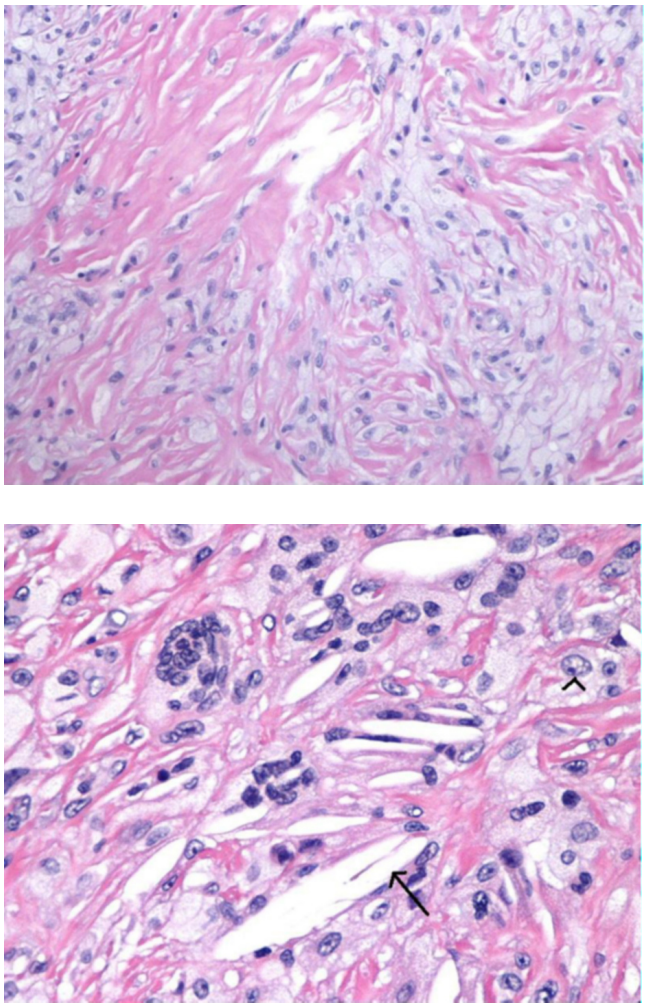

Figure 5. 38-year-old man with multitendon xanthomatosis. Photomicrographs of the resected extensor tendon from the middle finger. Top: Xanthomatous deposits with foam cells are interspersed with fibrous tissue (original magnification 200x; hematoxylin and eosin [H&E] stain). Above: Cholesterol clefts (arrowheads) and giant cells are adjacent to normal tendon cells (original magnification 400x; hematoxylin and eosin [H&E] stain).

the hereditary form of hypercholesterolemia. Their number and size correlate to some degree with the cholesterol level and the patient's age (4). Medical treatment is often delayed due to underdiagnosis. Frequently, the disease is suspected only by the findings of xanthomas on imaging. They usually cause no pain and do not increase the likelihood of tendon tears.

Nearly all cases of xanthomatosis are associated with either familial hypercholesterolemia or cerebrotendinous xanthomatosis (CTX). CTX is a rare autosomal-recessive, inherited, lipid-storage disease that is clinically characterized by cerebellar ataxia, spinal-cord involvement, premature atherosclerosis, cataracts, intellectual impairment, and peripheral neuropathy. The age of onset is variable, but symptoms usually occur in childhood, though they can also begin in the second or third decade (6). The tendon xanthomata may precede the onset of neurological symptoms by decades. It has been suggested by A. Smithard et al. (7) that CTX should be suspected in patients presenting with bilateral Achilles tendon xanthomas and normal plasma lipid levels. Our case demonstrates unilateral Achilles tendon involvement; however, no imaging was performed of the contralateral tendon to evaluate for subclinical involvement. Our patient was not specifically evaluated for CTX and was not recommended to undergo brain or spinal-cord imaging. However, he denies any referrable symptoms or family history. He is an active surgeon. Rarely, as in our case, xanthomas can be seen with a relatively normal standard metabolic panel. In such cases, the underlying process may be an abnormality of cholesterol subparticles, for example, apolipoprotein B. Therefore, more thorough metabolic testing may be indicated (8). Our patient refused any further evaluation, however.

Xanthomas may occasionally be confused with an entity referred to as fibrous xanthomas of the synovium (2). These are solitary lesions found near synovial sheaths. However, they do not infiltrate the tendon, are not typically found about large tendons, and are not familial. Microscopically, they can be similar. However, cholesterol clefts are rarely present in fibrous xanthomas (2).

MRI and sonography are well suited to the evaluation of tendons and soft-tissue masses. The MRI features of Achilles-tendon involvement with xanthomas have been described. In more dramatic cases, the involved tendon is enlarged and demonstrates abnormal configuration and signal pattern. The following findings on T1- and T2-weighted MRI are highly associated with xanthomatosis: 1) vertical striations of increased signal intensity interposed between the low-signal tendon fibers; 2) a more diffuse stippled or speckled appearance within an enlarged tendon. These findings are thought to be due to high signal foamy histiocytes and inflammatory reaction [9]. According to Dussault et al., MRI can assess changes before the tendon enlarges or the xanthomas become clinically detectable (9). In such cases, the tendon can have abnormal signal with this stippled pattern. Its value would be in establishing the diagnosis of familial hypercholesterolemia earlier in patients with hypercholesterolemia, in an attempt to retard or prevent atherosclerotic disease. However, overlap in diagnosis by MRI includes trauma, partial tendon tear, tendon hypoxic degeneration/tendinopathy, and involvement with rheumatoid arthritis and gout (10). Complete tears should not create a diagnostic dilemma.

Sonographically, Achilles-tendon involvement can show focal hypoechoic lesions compatible with xanthomas with

improved contrast resolution compared with MRI which demonstrate a more diffuse speckled or reticulated pattern (12). The tendons on sonography can appear as normal or, more commonly, enlarged. They demonstrate loss of the normal fibrillar architecture and either focal or diffuse hypoechogenicities within the tendon compatible with xanthomas (11).

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